REMARKS

I. Status of the Claims

Claims 1-18 are pending in the application, are under examination, and stand rejected, variously, under 35 U.S.C. §112, first and second paragraphs, 35 U.S.C. §102, 35 U.S.C. §103, and for alleged double-patenting. The specific grounds for rejection, and applicants' response thereto, are set out in detail below.

II. Rejection Under 35 U.S.C. §112, First Paragraph

Claims 1-12 and 14-17 stand rejected as lacking an adequate written description. In particular, the examiner questions whether one of ordinary skill in the art would find that the inventors were, at the time of filing, in possession of the genus of all bacteriophage tail proteins. Applicants traverse, but in the interest of advancing the prosecution, the claims have been amended to recite "p12 or p12-similar bacteriophage tail proteins." These proteins are described in the specification as those tail proteins binding to highly conserved regions of endotoxin, such as the core region or lipid A (page 11, lines 23-31). Reconsideration and withdrawal of the rejection is therefore respectfully requested.

III. Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 1-18 are rejected as indefinite. Applicants traverse, and provide the following in response to each rejection.

Claims 1 and 4. The examiner questions whether one or multiple proteins/complexes are being used/detected. Applicants have amended the claim to recite that these elements are

singular, but as the claim uses the transitional language of "comprising," in fact, it covers both embodiments.

Claims 4, 7 and 10. The claims are said to be indefinite in the use of the term "permanent carrier." This term is defined at page 12, lines 15-18, and in claim 6. However, in the interest of advancing the prosecution, the claim have been amended to recite the permanent carriers of claim 6.

Claim 6. The term "centrifugation material" is argued to be indefinite. Claim 6 has been canceled.

Claim 12. The dependency of this claim on claim 11 was said to create limitation problems with regard to tags. The claim has been amended to depend from claim 1, thereby obviating the rejection.

Claim 13. Claim 13 is said to lack antecedent basis for "p12 protein of the phage T4." The claim has been amended to address the examiner's concerns.

Claim 14. The claim is said to lack antecedent basis for "Ca^{2+} concentration ... and the Mg^{2+} concentration." An amendment is provided that is believed to address the examiner's concerns.

Claim 15. The claim is said to be confusing with regard to marked endotoxin. Applicants submit that the displacement approach relies on the concept that the carrier is coated with bacteriophage tail proteins which have already bound a marked endolysin. If the sample is now added, this fluorescently-labeled endotoxin will be replaced to a certain extent by endotoxin from the sample due to steady state kinetics. Thus, the amount of fluorescently labeled endotoxin in the sample is via steady state kinetics an indirect measure for the amount of (unlabeled) endotoxin bonded to the bacteriophage tail proteins on the carrier. With this understanding,

applicants have amended claim 15 to clarify the claimed subject matter. Support for this amendment can be found on page 12, lines 3-5, and page 15, lines 20-22.

Reconsideration and withdrawal of each of the foregoing claims is thus respectfully requested.

IV. Rejections Under 35 U.S.C. §102

A. Suzuki *et al.*

Claims 1-4, 7, 10, 11 and 15 are rejected as anticipated by Suzuki *et al.* Applicants traverse. As presented for reconsideration, all of the claims recite the presence of bivalent ions in the incubation step. Suzuki *et al.* fails to disclose the presence of bivalent ions in the incubation step. In fact, Suzuki *et al.* discloses the use of TBS (page 97, right column, last paragraph) for the incubation. Thus, this recitation is not met by the cited methods. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

B. Baxa *et al.*

Claims 1-3 and 15 are rejected as anticipated by Baxa *et al.* Applicants traverse. As presented for reconsideration, all of the claims recite the presence of bivalent ions in the incubation step. Baxa *et al.* fails to disclose the presence of bivalent ions in the incubation step. In fact, Baxa *et al.* describe the use of phosphate buffer (page 2041, right column, Endorhamnosidase assay) for the incubation. Thus, this recitation is not met by the cited methods. Reconsideration and withdrawal of the rejection is therefore respectfully requested.

V. Rejections Under 35 U.S.C. §103

A. Miller

Claims 1-4, 6-8, 10 and 15 are said to be obvious over Miller (U.S. Patent 7,087,376; "the '376 patent"). Applicants traverse.

The '376 patent does not teach a method for detecting endotoxin nor a method for removing endotoxin, as presently claimed. Rather, it relates to a method to detect bacteria using bacteriophage or bacteriophage proteins ('376 patent, col. 1, Field of the Invention, l. 12-25). It would not have been obvious to one of ordinary skill in the art to use the method disclosed in the '376 patent to detect or remove endotoxin. The fact that the '376 patent discloses that T4p12 is suited to bind bacteria is in no way an indication that T4p12 can serve as tool to detect or remove endotoxin. The '376 patent discloses that phages bind the corresponding receptors of the bacteria resulting in a protein-protein or protein-carbohydrate, or protein-lipid interaction ('376 patent, col. 3, l. 40-42). This generally indicates that protein, carbohydrates or lipids in the membrane are bound, but no further details disclosed.

It is not understood how this disclosure could, in any way, motivate the skilled artisan to detection and remove of endotoxin. The mere fact that endotoxin is present in the outer membrane of Gram-negative bacteria does not indicate that this it is bound by T4p12. In contrast, the inventors have provided the insight that that p12 and p12-similar phage tail proteins bind to the core of enterobacterial polysaccharides, and are therefore highly suited to detect and remove endotoxin (see FIGS. 6 and 7, and Example 12). This fact was not known from nor suggested by the teachings of the '376 patent. Hence, there could be no motivation to use p12 or p12-similar proteins to detect or remove endotoxin in the '376 patent. Consequently, the subject matter as presently claimed is not obvious over this reference.

Reconsideration and withdrawal of the claimed invention is therefore respectfully requested.

B. Baxa *et al.* in view of Sun *et al.*

Claims 4-6, 7 and 9 are rejected as obvious over Baxa *et al.* in view of Sun *et al.* Applicants traverse.

In particular, neither Baxa *et al.* nor Sun *et al.* disclose the use of bivalent ions in the incubation step. In addition, neither Baxa *et al.* nor Sun *et al.* disclose p12 or p12-similar bacteriophage tail proteins. Thus, even the combined teachings of these references fails to present each element of the claimed invention, and thus cannot render any of the present claim obvious.

Reconsideration and withdrawal of the claimed invention is therefore respectfully requested.

VI. Double-Patenting

A. Same Invention

The examiner has indicated that claims 11-13 are considered substantial duplicates of claims 16-18, and will be objected to if found allowable. Given the amendments made to render claims 16-18 dependent from claim 4, it is believed that the rejection is now moot.

B. Obviousness-Type

The examiner raises five different non-statutory double-patenting rejections, four of these being provisional. Because the first allowed case should be passed to issue prior to any

rejections being maintained, applicants thus need not address those rejections until at least one of the applications is allowed.

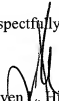
As for the rejection over the '376 patent, applicants have already pointed that even looking at the entire content of that document, it does not teach a method for detecting endotoxin nor a method for removing endotoxin, as presently claimed. At best, it relates to a method to detect bacteria using bacteriophage or bacteriophage proteins, and it would not have been obvious to one of ordinary skill in the art to use the method disclosed in the '376 patent to detect or remove endotoxin. When the analysis is limited further to the ***claims*** of the '376 patent, as must be done here, applicants again submit that this disclosure is clearly to insufficient to motivate the skilled artisan to detection and remove of endotoxin. Again, it is the inventors have provided the necessary insight that that p12 and p12-similar phage tail proteins bind to the core of enterobacterial polysaccharides, and are therefore highly suited to detect and remove endotoxin (see FIGS. 6 and 7, and Example 12). As such, the subject matter as presently claimed is not obvious over the claims of the '376 patent.

Reconsideration and withdrawal of the claimed invention is therefore respectfully requested.

VII. Conclusion

In light of the foregoing, applicants respectfully submit that all claims are in condition for allowance, and an early notification to that effect is earnestly solicited. The examiner is invited to contact the undersigned attorney at 512-536-3184 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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